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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,403	08/12/1999	WILLIAM R. ARATHOON	P1099C1	2534

23552 7590 02/07/2007  
MERCHANT & GOULD PC  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903

EXAMINER
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HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
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1643

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

**Application No.**

09/373,403

**Applicant(s)**

ARATHOON ET AL.

**Examiner**

Anne L. Holleran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 30-38, 40-43, 45-51 and 53-55 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30-38, 40-43, 45-51 and 53-55 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. The amendment filed 11/20/2006 is acknowledged. Claim 39 was canceled.  
Claims 30-38, 40-43, 45-51 and 53-55 are pending and examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claims Rejections/Objections Withdrawn:***

3. The provisional rejection of claims 30-43, 45- 51 and 53-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 88-109 of copending Application No. 09/863,693 is withdrawn in view of the abandonment of 09/863,693.
4. The rejection of claim 51 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment to claim 51.
5. The rejection of claims 30-42 under 35 U.S.C. 112, first paragraph, on the grounds that the applicants were not in possession of the claimed inventions at the time of filing, because the disclosure of the specification fails to adequately describe the claimed genus of compounds to be made in the claimed methods and encoded by the nucleic acids of the claimed host cells is withdrawn in view of the amendments to the claims.

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6. The objection to claim 39 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the cancellation of the claim.

7. The rejection of claims 30-43, 45-49, 50, 51 and 53-55 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

***Claim Rejections/Objections Maintained:***

8. The provisional rejection of claims 30-38, 40-43, 45- 51 and 53-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47-63 of copending Application No. 09/520,130 is maintained for the reasons of record. Applicants' request that the rejection be held in abeyance until notice of allowable subject matter is acknowledged.

9. The provisional rejection of claims 30-38, 40-43, 45- 51 and 53-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 45-82 of copending Application No. 10/143,437 is maintained for the reasons of record. Applicants' request that the rejection be held in abeyance until notice of allowable subject matter is acknowledged.

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10. Claims 30, 40, 41, 50 and 51 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nissim (Nissim, A. et al., The EMBO Journal, 13(3): 692-698, 1994; cited in IDS) as evidenced by Merchant (Merchant, A.M. et al, Nature Biotechnology, 16: 677-681, 1998; cited in IDS).

Nissim teaches methods for expressing scFv fragments in *E. coli* from a phage library. Merchant teaches that the phage library of Nissim is a library that has extensive H chain repertoires and unique L chain sequence, thus each antibody fragment derived from the phage library of Nissim has the same L chain. Nissim also teaches the making of “polyclonal” supernatants, which appear to be supernatants that contain scFv fragments with multiple specificities. In addition, Nissim teaches that multimerization occurs in the supernatants, especially when the supernatant has been concentrated (see 695, 2<sup>nd</sup> column). Nissim teaches that for polyclonal scFv fragments, the supernatant was concentrated. The multimerization appears to occur through the binding of an L chain region from one chain binding to an H chain region from another chain. Therefore, Nissim teaches the claimed methods of producing multispecific antibodies. Nissim also teaches the isolated host cells of claim 41, because Nissim teaches how to make the *E. coli* that produce the scFv fragments (see page 697, 2<sup>nd</sup> column). Therefore, Nissim teaches that claimed inventions.

***Response to Arguments:***

The rejection of claim 43 has been withdrawn upon further consideration, because claim 43 is drawn to a method with an active step of “selecting” nucleic acids. In contrast, claims 30 and 50 are broadly drawn to methods comprising culturing host cells that comprise nucleic acids

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encoding the first and additional polypeptides. Nissim teaches such host cells and teaches culturing such host cells and making multimerized, polyspecific antibody products by concentration of the host cell supernatant. Therefore, Nissim teaches a method that is the same as that claimed. Applicants argue that Nissim fails to teach a method making multispecific antibodies that comprise a multimerization domain. However, in the broadest interpretation, because claims 30 and 50 do not characterize by structure the multimerization domain, these claims read on diabodies where the interaction between the two scFvs is through the interaction of the heavy and light chain variable domains. Diabodies are formed by the binding of a light chain variable domain from one scFv binding with a heavy chain variable domain of a second scFv, and the binding of the light chain variable domain from the second scFv with the heavy chain variable domain of the first scFv. Therefore, it appears that Nissim's "polyclonal" multimerized products are multispecific, and because Nissim uses an scFv library with only one light chain, the products are the same as that claimed.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran  
Patent Examiner  
February 1, 2007



**LARRY R. HELMS, PH.D.**  
**SUPERVISORY PATENT EXAMINER**